```
Welcome to DIALOG

Dialog level 05.12.03D

? b 411;set files allscience
    08nov06 08:56:26 User219511 Session D662.2
       $0.00   0.100 DialUnits File410
   $0.00  Estimated cost File410
   $0.03  TELNET
   $0.03  Estimated cost this search
   $0.45  Estimated total session cost   0.221 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
  (c) 2006 Dialog

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
  You have 297 files in your file list.
  (To see banners, use SHOW FILES command)
? s noggin and fibrodysplasia

Your SELECT statement is:
  s noggin and fibrodysplasia

      Items  File
      -----  ----
         19    5: Biosis Previews(R)_1969-2006/Nov W1
          2   20: Dialog Global Reporter_1997-2006/Nov 08
          1   24: CSA Life Sciences Abstracts_1966-2006/Sep
         26   34: SciSearch(R) Cited Ref Sci_1990-2006/Oct W5
          4   45: EMCare_2006/Oct W5
          2   65: Inside Conferences_1993-2006/Nov 07
          3   71: ELSEVIER BIOBASE_1994-2006/Nov W1
         13   73: EMBASE_1974-2006/Nov 08
    Examined  50 files
          1   91: MANTIS(TM)_1880-2006/Jan
          1  107: Adis R&D Insight_1986-2006/Sep W1
          1  128: PHARMAPROJECTS_1980-2006/Oct W4
          1  135: NewsRx Weekly Reports_1995-2006/Oct W5
          7  144: Pascal_1973-2006/Oct W3
         12  155: MEDLINE(R)_1950-2006/Nov 06
    Examined 100 files
    Examined 150 files
          1  340: CLAIMS(R)/US Patent_1950-06/Nov 02
          1  348: EUROPEAN PATENTS_1978-2006/ 200644
         11  349: PCT FULLTEXT_1979-2006/UB=20061102UT=20061026
          2  357: Derwent Biotech Res.__1982-2006/Nov W2
          1  393: Beilstein Abstracts_2006/Q3
          2  399: CA SEARCH(R)_1967-2006/UD=14520
         26  440: Current Contents Search(R)_1990-2006/Nov 08
          1  445: IMS R&D Focus_1991-2006/Oct W1
          4  449: IMS Company Profiles_1992-2006/Aug
    Examined 200 files
    Examined 250 files
          9  654: US Pat.Full._1976-2006/Nov 07

  24 files have one or more items; file list includes 297 files.

? save temp; b 155,5,34,73;exs;rd
Temp SearchSave "TE323972985" stored
    08nov06 08:57:10 User219511 Session D662.3
       $2.97   1.119 DialUnits File411
   $2.97  Estimated cost File411
   $0.26  TELNET
   $3.23  Estimated cost this search
   $3.68  Estimated total session cost   1.341 DialUnits

SYSTEM:OS - DIALOG OneSearch
  File 155:MEDLINE(R) 1950-2006/Nov 06
       (c) format only 2006 Dialog
  File   5:Biosis Previews(R) 1969-2006/Nov W1
       (c) 2006 The Thomson Corporation
  File  34:SciSearch(R) Cited Ref Sci 1990-2006/Oct W5
       (c) 2006 The Thomson Corp
  File  73:EMBASE 1974-2006/Nov 08
       (c) 2006 Elsevier B.V.

      Set  Items  Description
      ---  -----  -----------
Executing TE323972985
HILIGHT set on as '%'
          3138  NOGGIN
          1223  FIBRODYSPLASIA
      S1    70  NOGGIN AND FIBRODYSPLASIA
      S2    38  RD  (unique items)
? t s2/7/1-38;bye

 2/7/1    (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

20000448  PMID: 15959366
   Developmental anomalies of the cervical spine in patients with
%fibrodysplasia% ossificans progressiva are distinctly different from those
in patients with Klippel-Feil syndrome: clues from the BMP signaling
pathway.
  Schaffer Alyssa A; Kaplan Frederick S; Tracy Michael R; O'Brien Megan L;
Dormans John P; Shore Eileen M; Harland Richard M; Kusumi Kenro
  Division of Orthopaedic Surgery, Children's Hospital of Philadelphia,
Institution B, Philadelphia, PA, USA.
  Spine (United States)  Jun 15 2005,  30 (12) p1379-85,  ISSN 1528-1159
--Electronic  Journal Code: 7610646
  Contract/Grant No.: 2R01-AR041916; AR; NIAMS
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  STUDY DESIGN: A radiographic analysis of the cervical spine of 70
patients diagnosed with %fibrodysplasia% ossificans progressiva (FOP) and
33 diagnosed with Klippel-Feil (KF) syndrome was conducted. OBJECTIVES: The
objectives of this study were to describe cervical spine abnormalities in
patients with FOP, to compare and contrast those findings with the
malformations in patients with KF syndrome, and to examine the possible
etiology of these abnormalities. SUMMARY OF BACKGROUND DATA: Congenital
features of diseases often provide seminal clues to underlying etiology and
developmental pathways. While progressive metamorphosis of connective
tissue to heterotopic bone is the most dramatic and disabling feature of
FOP, less severe congenital anomalies of the skeleton are also present.
Vertebral fusions observed in KF are consistent with defects in embryonic
segmentation. METHODS: The cervical spine plain films of 70 FOP patients
and 33 KF patients with documented congenital abnormalities were reviewed.
RESULTS: Generalized neck stiffness and decreased range of motion were
noted in most children with FOP. In the FOP patient group, characteristic
anomalies, including large posterior elements, tall narrow vertebral
bodies,and fusion of the facet joints between C2 and C7, were observed.
Most notably, these characteristic anomalies of the cervical spine in
patients with FOP were distinctly different from those of 33 patients with
KF that were examined but were strikingly similar to those seen in mice
with homozygous deletions of the gene-encoding %noggin%, a bone
morphogenetic protein (BMP) antagonist. CONCLUSIONS: FOP patients exhibit a
characteristic set of congenital spine malformations. While the %noggin%
gene (NOG) is not mutated in patients who have FOP, these findings extend a
growing body of evidence implicating overactivity of the BMP signaling
pathway in the molecular pathogenesis of FOP.
  Record Date Created: 20050616
  Record Date Completed: 20060228
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2/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

19706418 PMID: 16080294
A new mutation of the %noggin% gene in a French %Fibrodysplasia% ossificans progressiva (FOP) family.
Fontaine K; Semonin O; Legarde J P; Lenoir G; Lucotte G
European Sequence Gene, Cybergene, Evry, France.
Genetic counseling (Geneva, Switzerland) (Switzerland) 2005, 16 (2) p149-54, ISSN 1015-8146--Print Journal Code: 9015261
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
A new mutation of the %Noggin% gene in a French Fybrodysplasia ossificans progressiva (FOP) family: %Fibrodysplasia% ossificans progressiva (FOP) is a very rare disease characterized by congenital malformation of the great toes and progressive heterotopic ossification of the muscles. We previously located a FOP gene in the 17q21-22 region and described several mutations of the %noggin% (NOG) gene (located in 17q22) in four FOP patients, including the G91C mutation which is transmitted dominantly in a Spanish FOP family. We describe in the present study a new mutation of the NOG gene in a French FOP family. This new mutation is a guanine to adenine change at nucleotide 283 (283G --> A) of the NOG gene, and is transmitted in the family (in the heterozygote form) by the affected mother to her two affected children. At the peptide level this mutation (A95T) substitutes an Alanine residue by a Threonine at position 95 of the %Noggin% protein. The Alanine mutated residue is located just adjacent to the myristoylation site of the protein, where all the mutations we described until now are located.
Record Date Created: 20050805
Record Date Completed: 20060111

2/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

15105552 PMID: 15466378
Transgenic mice overexpressing BMP4 develop a %fibrodysplasia% ossificans progressiva (FOP)-like phenotype.
Kan Lixin; Hu Min; Gomes William A; Kessler John A
Department of Neurology, Northwestern University Feinberg School of Medicine, Ward Building 10-185, 303 East Chicago Avenue, Chicago, Illinois 60611-3008, USA. l-kan@northwestern.edu.
American journal of pathology (United States) Oct 2004, 165 (4) p1107-15, ISSN 0002-9440--Print Journal Code: 0370502
Contract/Grant No.: NS 20778; NS; NINDS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
%Fibrodysplasia% ossificans progressiva (FOP) is a rare hereditary connective tissue disease characterized by progressive postnatal heterotopic bone formation. Although the genetic defects of FOP are not known, several lines of evidence have suggested that bone morphogenetic protein-4 (BMP4) may be involved in the pathophysiology. Nevertheless BMP4-transgenic mice have previously failed to develop the disorder and there has been no good animal model of the disease. Here, we report that a unique transgenic mouse line that overexpresses BMP4 under control of the neuron-specific enolase (NSE) promoter develops a FOP-like phenotype. Mating of these animals with transgenic animals that overexpress the BMP inhibitor %noggin% prevents the disorder, confirming the role of BMP4 in the pathogenesis of the disease. Heterotopic bone formation in these animals appears to follow the classic endochondral ossification pathway. Sex-mismatched cell transplantation experiments indicate that multiple cell sources contribute to the heterotopic ossification. This remarkable animal model provides a unique opportunity to further study the role of the BMP signaling pathway in heterotopic ossification and to improve our understanding of the clinical aspects of FOP.
Record Date Created: 20041006
Record Date Completed: 20041103

2/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14624417 PMID: 14668502
In vivo somatic cell gene transfer of an engineered %Noggin% mutein prevents BMP4-induced heterotopic ossification.
Glaser David L; Economides Aris N; Wang Lili; Liu Xia; Kimble Robert D; Fandl James P; Wilson James M; Stahl Neil; Kaplan Frederick S; Shore Eileen M
Regeneron Pharmaceuticals, 777 Old Saw Mill River Road, Tarrytown, NY 10591, USA. david.glaser@uphs.upenn.edu
Journal of bone and joint surgery. American volume (United States) Dec 2003, 85-A (12) p2332-42, ISSN 0021-9355--Print Journal Code: 0014030
Contract/Grant No.: R01 AR 41916; AR; NIAMS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
BACKGROUND: The formation of the skeleton requires inductive signals that are balanced with their antagonists in a highly regulated negative feedback system. Inappropriate or excessive expression of BMPs (bone morphogenetic proteins) or their antagonists results in genetic disorders affecting the skeleton, such as %fibrodysplasia% ossificans progressiva. BMP signaling mediated through binding to its receptors is a critical step in the induction of abnormal ossification. Therefore, we hypothesized that engineering more effective inhibitors of this BMP-signaling process may lead to the development of therapies for such conditions. METHODS: BMP4-induced heterotopic ossification was used as a model for testing the ability of the BMP antagonist %Noggin% to block de novo bone formation, either by local or systemic delivery. Since %Noggin% naturally acts locally, a %Noggin% mutein, hNOGDeltaB2, was engineered and was shown to circulate systemically, and its ability to block heterotopic ossification was tested in a mouse model with use of adenovirus-mediated somatic cell gene transfer. RESULTS: A mouse model of BMP4-induced heterotopic ossification was developed. Local delivery of wild-type NOG inhibited heterotopic ossification, but systemic administration was ineffective. In contrast, systemic delivery of the adenovirus encoding hNOGDeltaB2 resulted in systemic levels that persisted for more than two weeks and were sufficient to block BMP4-induced heterotopic ossification. CONCLUSIONS: BMP4-induced heterotopic ossification can be prevented in vivo either by local delivery of wild-type %Noggin% or after somatic cell gene transfer of a %Noggin% mutein, hNOGDeltaB2. Furthermore, the data in the present study provide proof of concept that a naturally occurring factor can be engineered for systemic delivery toward a desirable pharmacological outcome. Clinical Relevance: Blocking bone formation is clinically relevant to disorders of heterotopic ossification in humans, such as %fibrodysplasia% ossificans progressiva. Furthermore, development of BMP antagonists as therapeutic agents may provide modalities for the treatment of other pathologic conditions that arise from aberrant expression of BMPs and/or from a lack of their antagonists.
Record Date Created: 20031211
Record Date Completed: 20040113

2/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14350566 PMID: 12804980
%Fibrodysplasia% ossificans progressiva.
Blaszczyk Maria; Majewski Slavomir; Brzezinska-Wcislo Ligia; Jablonska Stefania

Department of Dermatology and Venerology, Warsaw School of Medicine, 02-008 Warsaw, Koszykowa 82a str., Poland.
European journal of dermatology - EJD (France) May-Jun 2003, 13 (3) p234-7, ISSN 1167-1122--Print Journal Code: 9206420
Publishing Model Print
Document type: Case Reports; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
%Fibrodysplasia% ossificans progressiva, a rare genetic disabling disease characterized by heterotopic bone formation, is of special interest for general medicine since the bone morphogenetic proteins (especially BMP-4) involved in its pathogenesis are known to play a role in skeletal morphogenesis, and the gene antagonist to BMP-4 %noggin% might be useful in preventing lamellar bone formation. We present two cases with characteristic musculo-skeletal abnormalities and histopathological features (inflammatory infiltrates which destroyed muscle tissue replacing it by proliferating fibroblasts). In one patient due to high activity of fibroblasts, the histopathologic pattern appeared to be atypical and the lesion was recognized by a general pathologist as sarcoma. The other patient, due to the symmetrical induration of sternocleidomastoid muscles, was primarily recognized as scleredema. We stress the diagnostic importance of skeletal abnormalities (hallux valgus and others), and discuss differentiation from progressive osseous heteroplasia (POH) and congenital or acquired localized cutaneous and muscle ossifications which have a much better prognosis, as well as Albright's hereditary osteodystrophy, which differs by the presence of various systemic abnormalities. A study of FOP might provide an important clue to the genetic molecular mechanism of bone formation, development of heterotopic bone and a possible prevention by molecular manipulation with the gene responsible for bone morphogenetic proteins and their antagonists.
Record Date Created: 20030613
Record Date Completed: 20030930

2/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14244323 PMID: 12672843
Paresis of a bone morphogenetic protein-antagonist response in a genetic disorder of heterotopic skeletogenesis.
Ahn Jaimo; Serrano de la Pena Lourdes; Shore Eileen M; Kaplan Frederick S
University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA.
Journal of bone and joint surgery. American volume (United States) Apr 2003, 85-A (4) p667-74, ISSN 0021-9355--Print Journal Code: 0014030
Contract/Grant No.: 2-R01-AR41916; AR; NIAMS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
BACKGROUND: %Fibrodysplasia% ossificans progressiva is a rare genetic disorder characterized by congenital malformations of the great toes and by progressive heterotopic bone formation. Bone morphogenetic protein-4 (BMP-4) messenger ribonucleic acid (mRNA) and protein are uniquely overexpressed in lymphocytes and lesional cells from patients who have %fibrodysplasia% ossificans progressiva. However, the BMP-4 gene is not mutated in %fibrodysplasia% ossificans progressiva. The activities of BMPs are specified in part by the formation of morphogen gradients that are further regulated by an array of secreted antagonists. Recent studies have indicated that BMP-4 upregulates the expression of the BMP antagonists %noggin% , gremlin, and follistatin, thereby establishing an autoregulatory feedback loop. Therefore, a defect in the feedback pathway between BMP-4 and one or more of its extracellular antagonists could contribute to the elevated BMP-4 activity characteristic of %fibrodysplasia% ossificans progressiva. METHODS: Basal and BMP-4-induced expression of %noggin%, gremlin, follistatin, and chordin mRNA were investigated in control and %fibrodysplasia% ossificans progressiva lymphoblastoid cell lines with use of reverse transcriptase-polymerase chain reaction and Northern analysis. RESULTS: In the absence of exogenous BMP-4 stimulation (basal state), steady-state levels of all of the BMP antagonists that were investigated were similar in %fibrodysplasia% ossificans progressiva and control cell lines. Upon stimulation with recombinant human BMP-4, control lymphoblastoid cell lines exhibited a marked increase in expression of %noggin% and gremlin mRNA. %Fibrodysplasia% ossificans progressiva cells, however, showed a dramatically attenuated response to BMP-4 stimulation compared with that of controls. CONCLUSIONS: These data indicate a paresis of a BMP-antagonist response, suggesting the loss of a negative feedback mechanism by which cells normally regulate the magnitude and boundaries of ambient morphogenetic signals. This paresis may account in part for the increased BMP-4 activity in %fibrodysplasia% ossificans progressiva.
Record Date Created: 20030403
Record Date Completed: 20030527

2/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

13756947 PMID: 11977169
Significant difference of opinion regarding the role of %noggin% in %fibrodysplasia% ossificans progressiva.
Warman Matthew L
American journal of medical genetics (United States) Apr 22 2002, 109 (2) p162; author reply 163-4, ISSN 0148-7299--Print Journal Code: 7708900
Publishing Model Print; Comment on Am J Med Genet. 2001 Sep 1;102(4) 314-7; Comment on PMID 11503156
Document type: Comment; Letter
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Record Date Created: 20020523
Record Date Completed: 20020828

2/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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13756935 PMID: 11977155
Bone morphogenetic proteins with some comments on %fibrodysplasia% ossificans progressiva and %NOGGIN%.
Cohen M Michael
American journal of medical genetics (United States) Apr 22 2002, 109 (2) p87-92, ISSN 0148-7299--Print Journal Code: 7708900
Publishing Model Print
Document type: Editorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Record Date Created: 20020523
Record Date Completed: 20020828

2/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

13342120 PMID: 11503156
Identification of three novel mutations of the %noggin% gene in patients with %fibrodysplasia% ossificans progressiva.
Semonin O; Fontaine K; Daviaud C; Ayuso C; Lucotte G
E.S.G.S. Laboratory, Genopole site, Evry, France.
American journal of medical genetics (United States) Sep 1 2001, 102 (4) p314-7, ISSN 0148-7299--Print Journal Code: 7708900
Publishing Model Print; Comment in Am J Med Genet. 2002 Apr 22;109(2) 161; author reply 163-4; Comment in PMID 11977168; Comment in Am

J Med Genet. 2002 Apr 22;109(2):162; author reply 163-4; Comment in PMID 11977169
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
We report %noggin% mutations in three Spanish families with %fibrodysplasia% ossificans progressiva (FOP). The three propositi have typical FOP findings; in the first and third families the parents are unaffected, while in the second family the father is partially affected. DNA of the three propositi and their parents was screened by sequencing for mutations in the %noggin% gene (NOG). Sequencing indicated a G to C mutation at nucleotide 274 of the NOG gene in the first propositus, encoding for the G92R substitution at the peptide level; this first mutation is de novo, the corresponding change not being observed in parents. In the second propositus, a G to T mutation at nucleotide 271 encodes for the G91C substitution, transmitted in the corresponding family by the partially affected father. In the third propositus, sequencing indicated a G to A mutation at nucleotide 275, encoding for the G92E substitution; this third mutation is de novo. All three mutations, as well as the Delta42 deletion already reported, resulted in the alteration of the portion of the NOG gene at positions 265-282, encoding for the potential N-myristoylation site at residues 89-GGGGGA-94. Copyright 2001 Wiley-Liss, Inc.
Record Date Created: 20010814
Record Date Completed: 20011025

2/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12989256 PMID: 11140409
Localization of the gene for %fibrodysplasia% ossificans progressiva (FOP) to chromosome 17q21-22.
Lucotte G; Bathelier C; Mercier G; Gerard N; Lenoir G; Semonin O; Fontaine K
Center of Molecular Neurogenetics, Faculty of Medicine, Rheims, France.
Genetic counseling (Geneva, Switzerland) (Switzerland) 2000, 11 (4) p329-34, ISSN 1015-8146--Print Journal Code: 9015261
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
%Fibrodysplasia% ossificans progressiva (FOP) is a very rare disease characterized by congenital malformation of the great toes and progressive heterotopic ossification of muscles. To identify the chromosomal localization of the FOP gene, we conducted a genomewide linkage analysis using seven affected families. The FOP phenotype is linked to markers located in the 17q21-22 region (LOD score of 3.41 at the recombination fraction theta = 0). Crossover events localize the putative FOP gene within a 12cM interval, bordered proximally by D17S809 and distally by D17S1838. %Noggin% (NOG) gene, located in 17q22, is an excellent candidate gene for FOP.
Record Date Created: 20010103
Record Date Completed: 20010215

2/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12931744 PMID: 11076054
Linkage exclusion and mutational analysis of the %noggin% gene in patients with %fibrodysplasia% ossificans progressiva (FOP).
Xu M Q; Feldman G; Le Merrer M; Shugart Y Y; Glaser D L; Urtizberea J A; Fardeau M; Connor J M; Triffitt J; Smith R; Shore E M; Kaplan F S
Department of Orthopaedic Surgery, The University of Pennsylvania School of Medicine, Philadelphia, USA.
Clinical genetics (DENMARK) Oct 2000, 58 (4) p291-8, ISSN 0009-9163 --Print Journal Code: 0253664
Contract/Grant No.: 2RO1-AR41916-04; AR; NIAMS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
%Fibrodysplasia% ossificans progressiva (FOP) is an extremely rare and disabling genetic disorder characterized by congenital malformation of the great toes and by progressive heterotopic endochondral ossification in predictable anatomical patterns. Although elevated levels of bone morphogenetic protein 4 (BMP4) occur in lymphoblastoid cells and in lesional cells of patients with FOP, mutations have not been identified in the BMP4 gene, suggesting that the mutation in FOP may reside in a BMP4-interacting factor or in another component of the BMP4 pathway. A powerful antagonist of BMP4 is the secreted polypeptide %noggin%. A recent case report described a heterozygous 42-bp deletion in the protein-coding region of the %noggin% gene in a patient with FOP. In order to determine if %noggin% mutations are a widespread finding in FOP, we examined 31 families with 1 or more FOP patients. Linkage analysis with an array of highly polymorphic microsatellite markers closely linked to the %noggin% gene was performed in four classically-affected multigenerational FOP families and excluded linkage of the %noggin% locus to FOP (the multipoint lod score was -2 or less throughout the entire range of markers). We sequenced the %noggin% gene in affected members of all four families, as well as in 18 patients with sporadic FOP, and failed to detect any mutations. Single-strand conformation polymorphism (SSCP) analysis of 4 of these patients plus an additional 9 patients also failed to reveal any mutations. Among the samples analyzed by SSCP and DNA sequencing was an independently obtained DNA sample from the identical FOP patient previously described with the 42-bp %noggin% deletion; no mutation was detected. Examination of the DNA sequences of 20 cloned %noggin% PCR products, undertaken to evaluate the possibility of a somatic mutation in the %noggin% gene which could be carried by a small subset of white blood cells, also failed to detect the presence of the reported 42-bp deletion. We conclude that mutations in the coding region of %noggin% are not associated with FOP.
Record Date Created: 20010205
Record Date Completed: 20010301

2/7/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12218526 PMID: 10665670
A de novo heterozygous deletion of 42 base-pairs in the %noggin% gene of a %fibrodysplasia% ossificans progressiva patient.
Lucotte G; Semonin O; Lutz P
Clinical genetics (DENMARK) Dec 1999, 56 (6) p469-70, ISSN 0009-9163--Print Journal Code: 0253664
Publishing Model Print
Document type: Case Reports; Letter
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Record Date Created: 20000223
Record Date Completed: 20000223

2/7/13 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.

0016192525 BIOSIS NO.: 200600537920
Response regarding the article "Overexpression of %noggin% inhibits BMP-mediated growth of osteolytic prostate cancer lesions", by Feeley et al.
AUTHOR: Feeley Brian T; Lieberman Jay R (Reprint)
AUTHOR ADDRESS: Univ Calif Los Angeles, David Geffen Sch Med, Dept

Orthopaed Surg, Los Angeles, CA 90095 USA**USA
AUTHOR E-MAIL ADDRESS: jlieberman@mednet.ucla.edu
JOURNAL: Bone (New York) 39 (3): p667 SEP 2006 2006
ISSN: 8756-3282
DOCUMENT TYPE: Letter; Editorial
RECORD TYPE: Citation
LANGUAGE: English

2/7/14 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0016192524 BIOSIS NO.: 200600537919
Regarding the article "Overexpression of %noggin% inhibits BMP-mediated growth of osteolytic prostate cancer lesions", by Feeley et al.
AUTHOR: Friedlaender Gary E (Reprint)
AUTHOR ADDRESS: Yale Univ, Sch Med, Dept Orthopaed and Rehabil, POB 208071, New Haven, CT 06520 USA**USA
AUTHOR E-MAIL ADDRESS: gary.friedlaender@yale.edu
JOURNAL: Bone (New York) 39 (3): p666 SEP 2006 2006
ISSN: 8756-3282
DOCUMENT TYPE: Letter; Editorial
RECORD TYPE: Citation
LANGUAGE: English

2/7/15 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0016068023 BIOSIS NO.: 200600413418
%Fibrodysplasia% ossificans progressiva: Report of a family
AUTHOR: Dumic M (Reprint); Matic T; Bilinovac Z; Potocki K
JOURNAL: Calcified Tissue International 78 (Suppl. 1): pS37 JAN 2006 2006
CONFERENCE/MEETING: 33rd European Symposium on Calcified Tissues Prague, CZECH REPUBLIC May 10 -14, 2006; 20060510
ISSN: 0171-967X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/16 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015364072 BIOSIS NO.: 200510058572
Cervical spine anomalies in patients with %fibrodysplasia% ossificans progressiva: Clues from the BMP signaling pathway.
AUTHOR: Schaffer A A (Reprint); Kaplan F S; Tracy M R; O'Brien M L; Dormans J P; Shore E M; Harland R M; Kusumi K
AUTHOR ADDRESS: Univ Penn, Ctr Res FOP and Related Disorders, Philadelphia, PA 19104 USA**USA
JOURNAL: Journal of Bone and Mineral Research 19 pS491 OCT 04 2004
CONFERENCE/MEETING: 26th Annual Meeting of the American-Society-for-Bone-and-Mineral-Research Seattle, WA, USA October 01 -05, 2004; 20041001
SPONSOR: Amer Soc Bone & Mineral Res
ISSN: 0884-0431
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/17 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014784036 BIOSIS NO.: 200400150697
TGF-beta signaling in human skeletal and patterning disorders.
AUTHOR: Serra Rosa (Reprint); Chang Chenbei
AUTHOR ADDRESS: Department of Cell Biology, University of Alabama, Birmingham, 1918 University Blvd, 310 MCLM, Birmingham, AL, 35294-0005, USA**USA
AUTHOR E-MAIL ADDRESS: rserra@cellbio.bhs.uab.edu
JOURNAL: Birth Defects Research 69 (4): p333-351 November 2003 2003
MEDIUM: print
ISSN: 1542-0752 _(ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Members of the transforming growth factor beta (TGF-beta) family of multifunctional peptides are involved in almost every aspect of development. Model systems, ranging from genetically tractable invertebrates to genetically engineered mice, have been used to determine the mechanisms of TGF-beta signaling in normal development and in pathological situations. Furthermore, mutations in genes for the ligands, receptors, extracellular modulators, and intracellular signaling molecules have been associated with several human disorders. The most common are those associated with the development and maintenance of the skeletal system and axial patterning. This review focuses on the mechanisms of TGF-beta signaling with special emphasis on the molecules involved in human disorders of patterning and skeletal development.

2/7/18 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014476933 BIOSIS NO.: 200300431777
Dysregulated BMP4 signaling in FOP lymphocytes.
AUTHOR: de la Pena L Serrano (Reprint); Billings P C (Reprint); Shore E M (Reprint); Kaplan F S (Reprint)
AUTHOR ADDRESS: Orthopaedic Surgery, University of Pennsylvania School of Medicine, Philadelphia, PA, USA**USA
JOURNAL: Journal of Bone and Mineral Research 17 (Suppl 1): pS303 September 2002 2002
MEDIUM: print
CONFERENCE/MEETING: Twenty-Fourth Annual Meeting of the American Society for Bone and Mineral Research San Antonio, Texas, USA September 20-24, 2002; 20020920
SPONSOR: American Society for Bone and Mineral Research
ISSN: 0884-0431 _(ISSN print)
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/19 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014254999 BIOSIS NO.: 200300213718
Myristoylation defect in the protein %noggin% can cause %fibrodysplasia% ossificans progressiva.
AUTHOR: Lucotte G (Reprint); Semonin O (Reprint); Fontaine K (Reprint)
AUTHOR ADDRESS: Center of Molecular Neurogenetics, Paris, France**France
JOURNAL: Calcified Tissue International 72 (3): p258 March 2003 2003
MEDIUM: print
CONFERENCE/MEETING: Second International Workshop on the Genetics of Bone Metabolism and Disease Davos, Switzerland February 15-18, 2003; 20030215
ISSN: 0171-967X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/20 (Item 8 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

0013692116 BIOSIS NO.: 200200285627
Reply to correspondence by Xu et al. and Warman
AUTHOR: Fontaine Karine; Semonin Olivier; Lucotte Gerard (Reprint)
AUTHOR ADDRESS: Centre de Neurogenetique Moleculaire, 44 Rue Monge, Paris, France**France
JOURNAL: American Journal of Medical Genetics 109 (2): p163-164 April 22, 2002 2002
MEDIUM: print
ISSN: 0148-7299
DOCUMENT TYPE: Letter
RECORD TYPE: Citation
LANGUAGE: English

2/7/21 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013692113 BIOSIS NO.: 200200285624
Reported %noggin% mutations are PCR errors
AUTHOR: Xu Mei-qi; Shore Eileen M; Kaplan Frederick S (Reprint)
AUTHOR ADDRESS: Department of Orthopaedic Surgery, University of Pennsylvania Medical Center, 3400 Spruce Street, Two Silverstein, Philadelphia, PA, 19104-4283, USA**USA
JOURNAL: American Journal of Medical Genetics 109 (2): p161 April 22, 2002 2002
MEDIUM: print
ISSN: 0148-7299
DOCUMENT TYPE: Letter
RECORD TYPE: Citation
LANGUAGE: English

2/7/22 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011326838 BIOSIS NO.: 199800121085
Encrypted morphogens of skeletogenesis: Biological errors and pharmacologic potentials
AUTHOR: Kaplan Frederick S (Reprint); Shore Eileen M
AUTHOR ADDRESS: Dep. Orthop. Surg., Hosp. Univ. Pennsylvania, Silverstein Two, 3400 Spruce St., Philadelphia, PA 19104, USA**USA
JOURNAL: Biochemical Pharmacology 55 (4): p373-382 Feb. 15, 1998 1998
MEDIUM: print
ISSN: 0006-2952
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Bone morphogenetic proteins (BMPs) are members of a class of ancient, highly conserved signalling molecules that play major roles in embryonic axis determination, organ development, tissue repair, and regeneration throughout the animal kingdom. The bone morphogenetic proteins are potent developmental morphogens that act in a concentration-dependent manner to specify cell fates in developing and regenerating systems. Complementary DNAs have been cloned for approximately twenty BMPs, and recombinant proteins have been produced for many of these genes. Transgenic and naturally occurring animal models demonstrate a wide variety of potential functions for BMP genes during development and tissue regeneration, and a wide range of pharmacologic effects are predicted from knock-out or over-expression of the BMP genes. %Fibrodysplasia% ossificans progressiva (FOP), a rare and devastating genetic disease of ectopic osteogenesis in humans, is associated with over-expression of at least one of the BMPs. The BMPs, their transmembrane receptors, their intracellular signal transducers, and their secreted antagonists hold great promise as pharmacologic agents in modulating a vast array of developmental and regenerative pathways in human diseases.

2/7/23 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

15661072 Genuine Article#: BFA92 Number of References: 44
Title: Dysregulation of the BMP-4 signaling pathway in %fibrodysplasia% ossificans progressiva
Author(s): Kaplan FS (REPRINT) ; Fiori J; De la Pena LS; Ahn J; Billings PC ; Shore EM
Corporate Source: Univ Penn,Sch Med, Dept Orthopaed Surg,Silverstein 2,3400 Spruce St/Philadelphia//PA/19104 (REPRINT); Univ Penn,Sch Med, Dept Orthopaed Surg,Philadelphia//PA/19104; Univ Penn,Sch Med, Dept Med,Philadelphia//PA/19104; Univ Penn,Sch Med, Dept Genet,Philadelphia//PA/19104; Univ Penn,Sch Med, Ctr Res FOP & Related Disorders,Philadelphia//PA/19104(frederick.kaplan@uphs.upenn.edu)
, 2006, V1068, P54-65
ISSN: 0077-8923 Publication date: 20060000
Publisher: BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD OX4 2DQ, OXEN, ENGLANDSKELETAL DEVELOPMENT AND REMODELING IN HEALTH, DISEASE, AND AGING
Series: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Language: English Document Type: ARTICLE
Abstract: Identification of gene mutations in Mendelian disorders is often determined by linkage analysis and positional cloning, an approach that is difficult for %fibrodysplasia% ossificans progressiva (FOP) due to a low reproductive fitness that results in a small number of multigenerational families showing inheritance of the disease. Altered signaling pathways can be investigated as a complementary method to identify the consequences of the mutated gene responsible for FOP and to identify potential therapeutic targets. Candidate signaling pathways for FOP are those that malfunctioning could account for the malformation of the great toes during embryonic development and could explain the postnatal progressive heterotopic endochondral ossification. Signaling pathways that fit these criteria are the BMP signaling pathway and its interacting pathways. A large body of data suggest that the BMP-4 signaling pathway is dysregulated in FOP.

2/7/24 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

15200429 Genuine Article#: 048TZ Number of References: 101
Title: The role of inhibitory molecules in fracture heating
Author(s): Dimitriou R; Tsiridis E; Carr I; Simpson H; Giannoudis PV (REPRINT)
Corporate Source: St Jamess Univ Hosp,Dept Traumat & Orthopaed,Beckett St/Leeds LS9 7TF/W Yorkshire/England/ (REPRINT); Univ Leeds,Sch Med, Acad Dept Trauma & Orthopaed Surg,Leeds LS2 9JT/W Yorkshire/England/; Univ Leeds,Inst Mol Med,Leeds LS2 9JT/W Yorkshire/England/; Univ Edinburgh,Sch Med, Acad Dept Trauma & Orthopaed Surg,Edinburgh EH8 9YL/Midlothian/Scotland/(pgiannoudi@aol.com)
Journal: INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED, 2006, V37 , 1 (APR), PS20-S29
ISSN: 0020-1383 Publication date: 20060400
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
Language: English Document Type: ARTICLE
Abstract: The balance between at[the signalling molecules involved in bone formation with their inhibitors and most importantly between BMPs and their antagonists is critical determinant of osteogenesis, and therefore of skeletal development, fracture repair, and bone remodelling. The main identified inhibitory molecules of the osteogenic lineage, either from studies during embryonic development or from in vitro and in vivo studies are presented in the herein study. Potential treatments using these molecules either alone or in combination with

BMPs to control the bone growth and overgrowth are already under investigation aiming in treatments that mimic as much as possible the natural process of bone generation in various situations including fracture heating, osteoporosis, and osteoarthritis and other metabolic disorders, in order to more closely resemble the original tissue. (C) 2006 Elsevier Ltd. All. rights reserved.

2/7/25 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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13080406 Genuine Article#: 847RJ Number of References: 35
Title: Heterotopic ossification
Author(s): Kaplan FS (REPRINT) ; Glaser DL; Hebela N; Shore EM
Corporate Source: Univ Penn,Med Ctr, Sch Med, Dept Orthopaed Surg,Silverstein 2,3400 Spruce St/Philadelphia//PA/19104 (REPRINT); Univ Penn,Med Ctr, Sch Med, Dept Orthopaed Surg,Philadelphia//PA/19104; Univ Penn,Med Ctr, Sch Med, Dept Med,Philadelphia//PA/19104; Univ Penn,Sch Med, Dept Genet,Philadelphia//PA/19104
Journal: JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, 2004, V12, N2 (MAR-APR), P116-125
ISSN: 1067-151X Publication date: 20040300
Publisher: AMER ACAD ORTHOPAEDIC SURGEONS, 6300 N RIVER ROAD, ROSEMENT, IL 60018-4262 USA
Language: English Document Type: ARTICLE
Abstract: Heterotopic ossification, the formation of bone in soft tissue, requires inductive signaling pathways, inducible osteoprogenitor cells, and a heterotopic environment conducive to osteogenesis. Little is known about the molecular pathogenesis of this condition. Research into two rare heritable and developmental forms, %fibrodysplasia% ossficans progressiva and progressive osseous heteroplasia, has provided clinical, pathologic, and genetic insights. In %fibrodysplasia% ossificans progressiva, overexpression of bone morphogenetic protein 4 and underexpression of multiple antagonists of this protein highlight the potential role of a potent morphogenetic gradient. Research on %fibrodysplasia% ossificans progressiva also has led to the identification of the genetic cause of progressive osseous heteroplasia: inactivating mutations in the alpha subunit of the gene coding for the stimulatory G protein of adenylyl cyclase. Better understanding of the complex developmental and molecular pathology of these disorders may lead to more effective strategies to prevent and treat other, more common forms of heterotopic ossification.

2/7/26 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

12378773 Genuine Article#: 760BQ Number of References: 29
Title: Ankylosis of the jaw in a patient with %fibrodysplasia% ossificans progressiva
Author(s): Herford AS (REPRINT) ; Boyne PJ; Linda L
Corporate Source: Loma Linda Univ,Sch Dent, Dept Oral & Maxillofacial Surg,Room 3306,11092 Anderson St/Loma Linda//CA/92350 (REPRINT); Loma Linda Univ,Sch Dent, Dept Oral & Maxillofacial Surg,Loma Linda//CA/92350
Journal: ORAL SURGERY ORAL MEDICINE ORAL PATHOLOGY ORAL RADIOLOGY AND ENDODONTICS, 2003, V96, N6 (DEC), P680-684
ISSN: 1079-2104 Publication date: 20031200
Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA
Language: English Document Type: ARTICLE
Abstract: A case of %fibrodysplasia% ossificans progressiva (FOP) is presented. This uncommon connective tissue disease tends to produce progressing ectopic osteogenesis. Because there are no reported curative procedures for TMJ ankylosis occurring in this condition, a palliative surgical approach is described. Etiology, diagnosis, and prognosis of the disease is reviewed. Recent research in BMP cytokine-induced bone repair may allow new approaches to treating this debilitating disease in the future.

2/7/27 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

12317787 Genuine Article#: 746XF Number of References: 0
Title: Incomplete myristoylation in the protein %noggin% can cause %Fibrodysplasia% ossificans progressiva
Author(s): Lucotte G; Fontaine K; Semonin O
Corporate Source: Ctr Mol Neurogenet,Paris//France/
Journal: BONE, 2003, V33, N5 (NOV), PS18-S18
ISSN: 8756-3282 Publication date: 20031100
Publisher: ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA
Language: English Document Type: MEETING ABSTRACT

2/7/28 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

11931832 Genuine Article#: 710KZ Number of References: 30
Title: Structural basis of BMP signaling inhibition by %noggin%, a novel twelve-membered cystine knot protein
Author(s): Groppe J (REPRINT) ; Greenwald J; Wiater E; Rodriguez-Leon J; Economides AN; Kwiatkowski W; Baban K; Affolter M; Vale WW; Belmonte JCI; Choe S
Corporate Source: Salk Inst Biol Studies,Struct Biol Lab,10010 N Torrey Pines Rd/La Jolla//CA/92037 (REPRINT); Salk Inst Biol Studies,Struct Biol Lab,La Jolla//CA/92037
Journal: JOURNAL OF BONE AND JOINT SURGERY-AMERICAN VOLUME, 2003, V85A, 3, P52-58
ISSN: 0021-9355 Publication date: 20030000
Publisher: JOURNAL BONE JOINT SURGERY INC, 20 PICKERING ST, NEEDHAM, MA 02192 USA
Language: English Document Type: ARTICLE
Abstract: Background: The activity of bone morphogenetic proteins (BMPs) is regulated extracellularly by several families of secreted, negatively-acting factors. These BMP antagonists participate in the control of a diverse range of embryonic processes, such as establishment of the dorsal-ventral axis, neural induction, and formation of joints in the developing skeletal system. The ongoing process of neurogenesis in the adult brain also requires inhibition of BMP ligand activity. To date, the three-dimensional structures of these antagonists as well as the nature of their interaction with ligand have remained unknown. Toward that end, we have determined the crystal structure of the antagonist %Noggin% bound to BMP-7.

Methods: The complex of the two homodimeric proteins was preformed, isolated by size exclusion chromatography, and crystallized at neutral pH. To probe the molecular interface of the complex and to quantitate the activity of a human mutant form, variant %Noggin% proteins were produced and their binding affinities were measured in vitro. The correlation between binding affinity and biological activity was examined with %Noggin%-soaked beads implanted in the developing chick limb bud.

Results and Conclusions: The structure of the complex reveals that %Noggin% inhibits BMP signaling by blocking the binding sites of both types of receptors (Type I and Type 11), mimicking their modes of binding. The affinity of %Noggin% variants for BMP-7 correlated well with the inhibition of BMP-induced chondrogenesis in the chick limb bud, confirming that %Noggin% acts by sequestering the ligand in an inactive state. Interestingly, the scaffold of %Noggin% was found to contain a cystine knot topology and protein fold similar to that of BMPs, indicating that ligand and antagonist may have evolved from a common ancestral gene.

Clinical Relevance: Mutations in the human %Noggin% locus (NOG) are associated with three similar yet distinct skeletal dysplasias: proximal symphalangism (SYM1), multiple synostoses syndrome (SYNS1), and tarsal-carpal coalition syndrome (TCC). The crystal structure of the %Noggin%:BMP-7 complex provides a structural context for interpreting the effects of missense mutations with respect to %Noggin% protein folding, stability, or activity. The structure also provides the basis for engineering variants of %Noggin% that may have therapeutic applications in the treatment of %fibrodysplasia% ossificans progressiva (FOP), a rare genetic disorder of connective tissue resulting from lymphocytic misexpression of BMPs.

2/7/29 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

11653937 Genuine Article#: 679PU Number of References: 54
Title: Craniofacial anomalies: Clinical and molecular perspectives
Author(s): Cohen MM (REPRINT)
Corporate Source: Dalhousie Univ,Dept Oral & Maxillofacial Sci,Halifax/NS B3H 3J5/Canada/ (REPRINT); Dalhousie Univ,Dept Oral & Maxillofacial Sci,Halifax/NS B3H 3J5/Canada/; Dalhousie Univ,Dept Pediat,Halifax/NS B3H 3J5/Canada/; Dalhousie Univ,Dept Epidemiol & Community Hlth,Halifax/NS B3H 3J5/Canada/; Dalhousie Univ,Dept Hlth Serv Adm,Halifax/NS B3H 3J5/Canada/; Dalhousie Univ,Dept Sociol & Social Anthropol,Halifax/NS B3H 3J5/Canada/
Journal: ANNALS ACADEMY OF MEDICINE SINGAPORE, 2003, V32, N2 (MAR), P 244-251
ISSN: 0304-4602 Publication date: 20030300
Publisher: ACAD MEDICINE SINGAPORE, 142 NEIL RD, REPUBLIC SINGAPORE 088871, SINGAPORE
Language: English Document Type: ARTICLE
Abstract: The first three disorders discussed are abnormalities of bone: too little bone in cleidocranial dysplasia caused by mutations in RUNX2; too much bone in %fibrodysplasia% ossificans progressiva with overexpression of BMP4; and abnormal bone in McCune-Albright syndrome and fibrous dysplasia caused by mutations in GNAS1. Disorders of the sonic hedgehog signaling network are discussed next, including holoprosencephaly and the nevoid basal cell carcinoma syndrome, the former being caused by sonic hedgehog (SHH) mutations and the latter being caused by patched mutations (PTCH).

2/7/30 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

11567455 Genuine Article#: 668FH Number of References: 241
Title: Bone morphogenetic proteins, their antagonists, and the skeleton
Author(s): Canalis E (REPRINT) ; Economides AN; Gazzerro E
Corporate Source: St Francis Hosp & Med Ctr,Dept Res,114 Woodland St/Hartford//CT/06105 (REPRINT); St Francis Hosp & Med Ctr,Dept Res,Hartford//CT/06105; Univ Connecticut,Sch Med,Farmington//CT/06030; Regeneron Pharmaceut Inc,Tarrytown//NY/10591
Journal: ENDOCRINE REVIEWS, 2003, V24, N2 (APR), P218-235
ISSN: 0163-769X Publication date: 20030400
Publisher: ENDOCRINE SOC, 4350 EAST WEST HIGHWAY SUITE 500, BETHESDA, MD 20814-4110 USA
Language: English Document Type: REVIEW
Abstract: Skeletal homeostasis is determined by systemic hormones and local factors. Bone morphogenetic proteins (BMP) are unique because they induce the differentiation of mesenchymal cells toward cells of the osteoblastic lineage and also enhance the differentiated function of the osteoblast. However, the activity of BMPs needs to be tempered by intracellular and extracellular antagonists. BMPs bind to specific receptors and signal by phosphorylating the cytoplasmic proteins mothers against decapentaplegic (Smad) 1 and 5, which form heterodimers with Smad 4, and after nuclear translocation regulate transcription. BMP antagonists can be categorized as pseudoreceptors that compete with signaling receptors, inhibitory Smads that block signaling, intracellular binding proteins that bind Smad 1 and 5, and factors that induce ubiquitination and proteolysis of signaling Smads. In addition, a large number of extracellular proteins that bind BMPs and prevent their binding to signaling receptors have emerged. They are the components of the Spemann organizer, %noggin%, chordin, and follistatin, members of the Dan/Cerberus family, and twisted gastrulation. The antagonists tend to be specific for BMPs and are regulated by BMPs, indicating the existence and need of local feedback mechanisms to temper BMP cellular activities.

2/7/31 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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11286443 Genuine Article#: 634EG Number of References: 33
Title: Exoneration of NF-kappa B dysregulation in %fibrodysplasia% ossificans progressiva
Author(s): Ahn J; Feldman G; Terry L; Shore EM; Kaplan FS (REPRINT)
Corporate Source: Hosp Univ Penn,Div Metab Bone Dis & Mol Orthopaed, Dept Orthopaed Surg,3400 Spruce St,Silverstein 2/Philadelphia//PA/19104 (REPRINT); Univ Penn,Sch Med, Dept Orthopaed Surg,Philadelphia//PA/19104; Univ Penn,Sch Med, Dept Genet,Philadelphia//PA/19104; Univ Penn,Sch Med, Dept Med,Philadelphia//PA/19104
Journal: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, 2003, N406 (JAN), P 205-213
ISSN: 0009-921X Publication date: 20030100
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA
Language: English Document Type: ARTICLE
Abstract: %Fibrodysplasia% ossificans progressiva is a disabling genetic disorder characterized by congenital skeletal malformations and progressive heterotopic ossification. New episodes of ossification are heralded by preosseous inflammatory lesions replete with B and T lymphocytes that overexpress bone morphogenetic protein-4. NF-kappaB is an inflammatory mediator that plays a critical role in developmental skeletogenesis and in suppression of bone morphogenetic protein-4 expression. Because of its multiple roles in inflammation, skeletogenesis, and bone morphogenetic protein-4 regulation, NF-kappaB may play an important functional role in the pathogenesis of %fibrodysplasia% ossificans progressiva. To clarify the potential role of NF-kappaB in the pathophysiologic features of %fibrodysplasia% ossificans progressiva, the role of NF-kappaB in regulating bone morphogenetic protein-4 signaling in patient-derived lymphoblastoid cell lines was examined. General NF-kappaB activity and specific NF-kappaB suppression of bone morphogenetic protein-4 expression were not altered in %fibrodysplasia% ossificans progressiva. In addition, despite the proximity of the gene for the p50 subunit of NF-kappaB (NFKB1 on long arm of chromosome 4) to the recently mapped locus for %fibrodysplasia% ossificans progressiva, a detailed linkage exclusion analysis in four multigenerational families with the disorder excluded NFKB1 as the causative gene for %fibrodysplasia% ossificans progressiva. These data exonerate NF-kappaB as the critical molecular and genetic pathogenic mediator in %fibrodysplasia% ossificans progressiva and, therefore, implicate a defect in another regulatory pathway as the cause for bone morphogenetic protein-4 overexpression in the disease.

2/7/32 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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09782307 Genuine Article#: 447ML Number of References: 28
Title: Inherited ectopic ossification: clinical lessons and biological insights
Author(s): Smith R (REPRINT)
Corporate Source: Nuffield Orthopaed Ctr,Windmill Rd,Headington/Oxford OX3

7LD//England/ (REPRINT); Nuffield Orthopaed Ctr,Oxford OX3 7LD//England/
Journal: CURRENT ORTHOPAEDICS, 2000, V14, N6 (NOV), P470-474
ISSN: 0268-0890 Publication date: 20001100
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND
Language: English Document Type: ARTICLE

2/7/33 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 The Thomson Corp. All rts. reserv.

09176952 Genuine Article#: 370KL Number of References: 0
Title: Localisation of the gene for %fibrodysplasia% ossificans progressiva (FOP) to chromosome 17q21-22 and %noggin% gene as candidate for FOP
Author(s): Lucotte G; Bathelier C; Mercier G; Lenoir G; Semonin O; Fontaine K
Corporate Source: FAC MED REIMS,GRP RECH FIBRODYSPLASIA OSSIFIANTE PROGRESS, CTR NEUROGENET MOL/REIMS//FRANCE/
Journal: DEVELOPMENTAL DYNAMICS, 2000, V219, N3 (NOV), PP29-P29
ISSN: 1058-8388 Publication date: 20001100
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012
Language: English Document Type: MEETING ABSTRACT

2/7/34 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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07918183 Genuine Article#: 224GJ Number of References: 38
Title: Phenotypic and molecular heterogeneity in %fibrodysplasia% ossificans progressiva
Author(s): Virdi AS; Shore EM; Oreffo ROC; Li M; Connor JM; Smith R; Kaplan FS; Triffitt JT (REPRINT)
Corporate Source: UNIV OXFORD,NUFFIELD DEPT ORTHOPAED SURG, MRC, BONE RES LAB, NUFFIELD ORTHOPAED CTR/OXFORD OX3 7LD//ENGLAND/ (REPRINT); UNIV OXFORD,NUFFIELD DEPT ORTHOPAED SURG, MRC, BONE RES LAB, NUFFIELD ORTHOPAED CTR/OXFORD OX3 7LD//ENGLAND/; UNIV PENN,SCH MED, LAB MOL ORTHOPAED, DEPT ORTHOPAED SURG/PHILADELPHIA//PA/19104; UNIV PENN,SCH MED, LAB MOL ORTHOPAED, DEPT MED/PHILADELPHIA//PA/19104; UNIV PENN,SCH MED, LAB MOL ORTHOPAED, DEPT GENET/PHILADELPHIA//PA/19104; DUNCAN GUTHRIE INST MED GENET,/GLASGOW G3 8SJ/LANARK/SCOTLAND/
Journal: CALCIFIED TISSUE INTERNATIONAL, 1999, V65, N3 (SEP), P250-255
ISSN: 0171-967X Publication date: 19990900
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010
Language: English Document Type: ARTICLE
Abstract: %Fibrodysplasia% (myositis) ossificans progressiva (FOP) is an extremely rare inherited disorder in which progressive ossification of major striated muscles, often following injury, is associated with abnormal skeletal patterning. Altered expression of bone morphogenetic proteins may be a contributory cause. To examine this hypothesis, we compared the patterns of expression of bone morphogenetic proteins (BMPs) mRNAs from lymphoblastoid cell lines from two small multigenerational families with autosomal dominant transmission of FOP. Although affected members of both families showed the characteristic phenotype of FOP, one family was more severely affected than the other. Expression of mRNAs for BMP-1, 2, 3, 5, and 6 mRNAs were not detected within the more severely affected family, but BMP-4 mRNA was expressed in affected but not unaffected members of this family. The results of linkage exclusion analysis using a highly polymorphic microsatellite marker near the BMP-4 gene were consistent with linkage of FOP and BMP-4 in this family. Within the less severely affected family, affected and unaffected members showed similar levels of mRNA expression of BMPs 1, 2, 4, and 5, and linkage of FOP to the BMP-4 gene was excluded. it is concluded that clinical, radiographic, and biochemical data in these two families with FOP establish clinical and molecular heterogeneity and also suggest the possibility of genetic heterogeneity.

2/7/35 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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12396141 EMBASE No: 2003500817
In Vivo Somatic Cell Gene Transfer of an Engineered %Noggin% Mutein Prevents BMPSUB4-Induced Heterotopic Ossification
Glaser D.L.; Economides A.N.; Wang L.; Liu X.; Kimble R.D.; Fandl J.P.; Wilson J.M.; Stahl N.; Kaplan F.S.; Shore E.M.
Dr. D.L. Glaser, Department of Orthopaedic Surgery, University of Pennsylvania, 424 Stemmler Hall, 36th and Hamilton Walk, Philadelphia, PA 19104-6081 United States
AUTHOR EMAIL: david.glaser@uphs.upenn.edu
Journal of Bone and Joint Surgery - Series A (J. BONE JT. SURG. SER. A) (United States) 2003, 85/12 (2332-2342)
CODEN: JBJSA ISSN: 0021-9355
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 61

Background: The formation of the skeleton requires inductive signals that are balanced with their antagonists in a highly regulated negative feedback system. Inappropriate or excessive expression of BMPs (bone morphogenetic proteins) or their antagonists results in genetic disorders affecting the skeleton, such as %fibrodysplasia% ossificans progressiva. BMP signaling mediated through binding to its receptors is a critical step in the induction of abnormal ossification. Therefore, we hypothesized that engineering more effective inhibitors of this BMP-signaling process may lead to the development of therapies for such conditions. Methods: BMP4-induced heterotopic ossification was used as a model for testing the ability of the BMP antagonist %Noggin% to block de novo bone formation, either by local or systemic delivery. Since %Noggin% naturally acts locally, a %Noggin% mutein, hNOGDELTAB2, was engineered and was shown to circulate systemically, and its ability to block heterotopic ossification was tested in a mouse model with use of adenovirus-mediated somatic cell gene transfer. Results: A mouse model of BMP4-induced heterotopic ossification was developed. Local delivery of wild-type NOG inhibited heterotopic ossification, but systemic administration was ineffective. In contrast, systemic delivery of the adenovirus encoding hNOGDELTAB2 resulted in systemic levels that persisted for more than two weeks and were sufficient to block BMP4-induced heterotopic ossification. Conclusions: BMP4-induced heterotopic ossification can be prevented in vivo either by local delivery of wild-type %Noggin% or after somatic cell gene transfer of a %Noggin% mutein, hNOGDELTAB2. Furthermore, the data in the present study provide proof of concept that a naturally occurring factor can be engineered for systemic delivery toward a desirable pharmacological outcome. Clinical Relevance: Blocking bone formation is clinically relevant to disorders of heterotopic ossification in humans, such as %fibrodysplasia% ossificans progressiva. Furthermore, development of BMP antagonists as therapeutic agents may provide modalities for the treatment of other pathologic conditions that arise from aberrant expression of BMPs and/or from a lack of their antagonists.

2/7/36 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
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11553692 EMBASE No: 2002125507
Significant difference of opinion regarding the role of %noggin% in %fibrodysplasia% ossificans progressiva [3] (multiple letters)
Warman M.L.; Fontaine K.; Semonin O.; Lucotte G.
Dr. M.L. Warman, Department of Genetics, BRB-719, Case Western Reserve Univ. Sch. Med., 2109 Adelbert Road, Cleveland, OH 44106 United States
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American Journal of Medical Genetics (AM. J. MED. GENET.) (United States) 22 APR 2002, 109/2 (162-164)

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DOCUMENT TYPE: Journal ; Letter
LANGUAGE: ENGLISH

2/7/37 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

11553678 EMBASE No: 2002125493
Bone morphogenetic proteins with some comments on %fibrodysplasia% ossificans progressiva and %NOGGIN%
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American Journal of Medical Genetics (AM. J. MED. GENET.) (United States) 22 APR 2002, 109/2 (87-92)
CODEN: AJMGD ISSN: 0148-7299
DOCUMENT TYPE: Journal ; Editorial
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 65

2/7/38 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

10564225 EMBASE No: 2000029205
A de novo heterozygous deletion of 42 base-pairs in the %noggin% gene of a %fibrodysplasia% ossificans progressiva patient [4]
Lucotte G.; Semonin O.; Lutz P.
Prof. G. Lucotte, Centre de Neurogenetique Moleculaire, Faculti de Medecine, 51 rue Cognacq-Jay, 51100 Reims Cedex France
Clinical Genetics (CLIN. GENET.) (Denmark) 1999, 56/6 (469-470)
CODEN: CLGNA ISSN: 0009-9163
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